

### **Abstract**

The present invention relates to novel antithrombotic variants of thrombin or fragments thereof that are capable of proteolytically activating protein C, but which are substantially free of fibrinogen cleavage activity. The present invention  
5 further relates to variant polypeptidess that may be cleaved to yield active thrombin variants. The present invention also relates to methods of inhibiting thrombus formation in an animal or human subject by delivering an antithrombotic variant thrombin of the present invention to the blood of the subject. The present invention relates also to methods that use the novel variant  
10 thrombins for determining the level of protein C activation in a blood sample, or the thrombogenic potential of a patient.